## SEQUENCE LISTING

<110> Saba, Julie D. Fyrst, Henrik

<120> SPHINGOSINE-1-PHOSPHATE LYASE POLYPEPTIDES, POLYNUCLEOTIDES AND MODULATING AGENTS AND METHODS OF USE THEREFOR

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aag Lys	aat Asn	cct Pro 515	Lys	gct Ala	aag Lys	acc Thr	aca Thr 520	Gly	atg Met	ggt Gly	gcc Ala	atc Ile 525	Tyr	ggc	atg Met	1584
gcc Ala	cag Gln 530	Ala	acc Thr	att Ile	gac Asp	agg Arg 535	Lys	ctg Leu	gtt Val	gca Ala	gaa Glu 540	ille	tcc Ser	tcc Ser	gtc Val	1632
ttc Phe 545	Leu	gac Asp	: tgc > Cys	ctt Lev	tat Tyr 550	Thr	acg Thr	gac Asp	ccc Pro	gto Val	. Thr	caç Glr	ı Gly	aac Asn	cag Gln 560	1680
atg Met	aac Asr	ggt Gly	tct Ser	cca Pro	aag Lys	cco Pro	cgc Arg	tga ; *	L							1707

<sup>&</sup>lt;210> 6 <211> 568

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Mus musculus

Met Pro Gly Thr Asp Leu Leu Lys Leu Lys Asp Phe Glu Pro Tyr Leu Glu Ile Leu Glu Ser Tyr Ser Thr Lys Ala Lys Asn Tyr Val Asn Gly 25 Tyr Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Leu 40 Cys Thr Leu Leu Ile Val Trp Val Tyr Glu Leu Ile Phe Gln Pro Glu 55 Ser Leu Trp Ser Arg Phe Lys Lys Lys Leu Phe Lys Leu Ile Arg Lys 75 70 Met Pro Phe Ile Gly Arg Lys Ile Glu Gln Gln Val Ser Lys Ala Lys 85 90 Lys Asp Leu Val Lys Asn Met Pro Phe Leu Lys Val Asp Lys Asp Tyr 100 105 Val Lys Thr Leu Pro Ala Gln Gly Met Gly Thr Ala Glu Val Leu Glu 120 Arg Leu Lys Glu Tyr Ser Ser Met Asp Gly Ser Trp Gln Glu Gly Lys 140 135 Ala Ser Gly Ala Val Tyr Asn Gly Glu Pro Lys Leu Thr Glu Leu Leu 150 155 Val Gln Ala Tyr Gly Glu Phe Thr Trp Ser Asn Pro Leu His Pro Asp 170 165 Ile Phe Pro Gly Leu Arg Lys Leu Glu Ala Glu Ile Val Arg Met Thr 190 185 180 Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser 205 200 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Tyr Arg Asp Leu 215 Ala Leu Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Glu Ser 230 235 Ala His Ala Ala Phe Asp Lys Ala Ala His Tyr Phe Gly Met Lys Ile 250 Val Arg Val Ala Leu Lys Lys Asn Met Glu Val Asp Val Gln Ala Met 265 260 Lys Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro 285 280 Gln Phe Pro His Gly Val Met Asp Pro Val Pro Glu Val Ala Lys Leu 295 300 Thr Val Arg Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly 315 Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu Lys Pro 330 325 Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His 345 Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Val Val Met Tyr Ser Asn 360 Glu Lys Tyr Arg Thr Tyr Gln Phe Phe Val Gly Ala Asp Trp Gln Gly 375 Gly Val Tyr Ala Ser Pro Ser Ile Ala Gly Ser Arg Pro Gly Gly Ile 395 390 Ile Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr 410 405 Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser 425

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Glu Leu Glu Asn Ile Lys Asn Ile Phe Ile Phe Gly Asp Pro Gln Leu
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        435
Ser Val Ile Ala Leu Gly Ser Asn Asp Phe Asp Ile Tyr Arg Leu Ser
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                        455
Asn Met Met Ser Ala Lys Gly Trp Asn Phe Asn Tyr Leu Gln Phe Pro
                                        475
                    470
Arg Ser Ile His Phe Cys Ile Thr Leu Val His Thr Arg Lys Arg Val
                                    490
                485
Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met
                                                     510
                                505
            500
Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met
                                                525
                            520
Ala Gln Ala Thr Ile Asp Arg Lys Leu Val Ala Glu Ile Ser Ser Val
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Phe Leu Asp Cys Leu Tyr Thr Thr Asp Pro Val Thr Gln Gly Asn Gln
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Met Asn Gly Ser Pro Lys Pro Arg
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                                                          15
                 5
gag att ttg gaa gta tac tcc aca aaa gcc aag aat tat gta aat gga
                                                                    96
Glu Ile Leu Glu Val Tyr Ser Thr Lys Ala Lys Asn Tyr Val Asn Gly
cat tgc acc aag tat gag ccc tgg cag cta att gca tgg agt gtc gtg
                                                                    144
His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val
tgg acc ctg ctg ata gtc tgg gga tat gag ttt gtc ttc cag cca gag
                                                                    192
Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu
                          55
                                                                    240
agt tta tgg tca agg ttt aaa aag aaa tgt ttt aag ctc acc agg aag
Ser Leu Trp Ser Arg Phe Lys Lys Lys Cys Phe Lys Leu Thr Arg Lys
                      70
 65
atg ccc att att ggt cgt aag att caa gac aag ttg aac aag acc aag
                                                                    288
Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys
                                      90
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gat Asp	gat Asp	att Ile	agc Ser 100	aag Lys	aac Asn	atg Met	tca Ser	ttc Phe 105	ctg Leu	aaa Lys	gtg Val	gac Asp	aaa Lys 110	gag Glu	tat Tyr	336
gtg Val	aaa Lys	gct Ala 115	tta Leu	ccc Pro	tcc Ser	cag Gln	ggt Gly 120	ctg Leu	agc Ser	tca Ser	tct Ser	gct Ala 125	gtt Val	ttg Leu	gag Glu	384
aaa Lys	ctt Leu 130	aag Lys	gag Glu	tac Tyr	agc Ser	tct Ser 135	atg Met	gac Asp	gcc Ala	ttc Phe	tgg Trp 140	caa Gln	gag Glu	ggg Gly	aga Arg	432
gcc Ala 145	tct Ser	gga Gly	aca Thr	gtg Val	tac Tyr 150	agt Ser	ggg Gly	gag Glu	gag Glu	aag Lys 155	ctc Leu	act Thr	gag Glu	ctc Leu	ctt Leu 160	480
gtg Val	aag Lys	gct Ala	tat Tyr	gga Gly 165	gat Asp	ttt Phe	gca Ala	tgg Trp	agt Ser 170	aac Asn	ccc Pro	ctg Leu	cat His	cca Pro 175	gat Asp	528
ato Ile	ttc Phe	cca Pro	gga Gly 180	cta Leu	cgc Arg	aag Lys	ata Ile	gag Glu 185	gca Ala	gaa Glu	att Ile	gtg Val	agg Arg 190	ata Ile	gct Ala	576
tgt Cys	tcc Ser	ctg Leu 195	ttc Phe	aat Asn	ggg	gga Gly	cca Pro 200	gat Asp	tcg Ser	tgt Cys	gga Gly	tgt Cys 205	gtg Val	act Thr	tct Ser	624
Gl <sup>7</sup> ggc	gga Gly 210	Thr	gaa Glu	agc Ser	ata Ile	ctc Leu 215	atg Met	gcc Ala	tgc Cys	aaa Lys	gca Ala 220	tgt Cys	cgg Arg	gat Asp	ctg Leu	672
gcc Ala 225	ttt Phe	gag Glu	aag Lys	Gly	atc Ile 230	Lys	act Thr	cca Pro	gaa Glu	att Ile 235	Val	gct Ala	ccc Pro	caa Gln	agt Ser 240	720
gco Ala	c cat a His	gct Ala	gca Ala	ttt Phe 245	Asn	aaa Lys	gca Ala	gcc Ala	agt Ser 250	Tyr	ttt Phe	ggg	atg Met	aag Lys 255	TTe	768
gto Val	g cgg L Arg	gtc Val	cca Pro 260	Leu	acg Thr	aag Lys	atg Met	atg Met 265	Glu	gtg Val	gat Asp	gtg Val	agg Arg 270	, Ala	atg Met	816
ag Ar	a aga g Arg	gct Ala 275	Ile	tcc Ser	agg Arg	aac Asn	act Thr 280	Ala	atg Met	ctc Leu	gtc Val	tgt Cys 285	Ser	acc Thr	cca Pro	864
Gl:	g ttt n Phe 290	e Pro	) His	Gly	v Val	. Ile 295	Asp	Pro	val	. Pro	300	ı Val	. Ala	а Lys	: Leu	912
gc Al	t gto a Val	c aaa L Lys	tac Tyr	aaa Lys	ata Ile	a ccc e Pro	ctt Lei	cat u His	gto Val	gac Asp	gct Ala	tgt a Cys	cto Lei	g gga ı Gly	ggc Gly	960

305					310				315					320	
ttc (			~		_		_				_				1008
ttt q Phe <i>I</i>															1056
aag t Lys :															1104
aag a Lys l	_					_		-			_	_			1152
ggc 8 Gly 3 385			~				_								1200
agc (	_	_	_		_	_	 								1248
gtt ( Val (															1296
gaa ( Glu )	_	_						-							1344
tca ( Ser 1															1392
aac ( Asn 1 465	_	_		_	_			_		_	_	_			1440
ccc a	_				_					_			_	_	1488
gct a Ala I															1536
aag a Lys <i>l</i>															1584

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gcc cag aca act gtt gac agg aat atg gtt gca gaa ttg tcc tca gtc
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Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val
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ttc ttg gac agc ttg tac agc acc gac act gtc acc cag ggc agc cag
                                                                 1680
Phe Leu Asp Ser Leu Tyr Ser Thr Asp Thr Val Thr Gln Gly Ser Gln
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His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val
                                               45
                           40
Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu
                                           60
Ser Leu Trp Ser Arg Phe Lys Lys Lys Cys Phe Lys Leu Thr Arg Lys
                                       75
Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys
                                    90
                85
Asp Asp Ile Ser Lys Asn Met Ser Phe Leu Lys Val Asp Lys Glu Tyr
                               105
Val Lys Ala Leu Pro Ser Gln Gly Leu Ser Ser Ser Ala Val Leu Glu
                                           125
                           120
Lys Leu Lys Glu Tyr Ser Ser Met Asp Ala Phe Trp Gln Glu Gly Arg
                                           140
                        135
Ala Ser Gly Thr Val Tyr Ser Gly Glu Glu Lys Leu Thr Glu Leu Leu
                                       155
                    150
Val Lys Ala Tyr Gly Asp Phe Ala Trp Ser Asn Pro Leu His Pro Asp
                                   170
                165
Ile Phe Pro Gly Leu Arg Lys Ile Glu Ala Glu Ile Val Arg Ile Ala
                                                   190
                                185
            180
 Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser
                            200
        195
 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Cys Arg Asp Leu
                                            220
                        215
 Ala Phe Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Gln Ser
                                        235
                    230
 Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile
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                245
 Val Arg Val Pro Leu Thr Lys Met Met Glu Val Asp Val Arg Ala Met
             260 265
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Arg Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro

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280
                                              285
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Gln Phe Pro His Gly Val Ile Asp Pro Val Pro Glu Val Ala Lys Leu
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                                         300
Ala Val Lys Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly
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                                   315
Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu His Pro
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                                   330
Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His
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                              345
Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Leu Val Leu Tyr Ser Asp
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Lys Lys Tyr Arg Asn Tyr Gln Phe Phe Val Asp Thr Asp Trp Gln Gly
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Gly Ile Tyr Ala Ser Pro Thr Ile Ala Gly Ser Arg Pro Gly Gly Ile
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                                      395
Ser Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr
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                                  410
Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser
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Glu Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu
                          440
                                             445
Ser Leu Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser
                      455
                             460
Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro
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                        475
Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val
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                                  490
Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met
                               505
Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Ala Met
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Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val
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gag att ttg gaa gta tac tcc aca aaa gcc aag aat tat gta aat gga

Glu	Ile	Leu	Glu 20	Val	Tyr	Ser	Thr	Lys 25	Ala	Lys	Asn	Tyr	Val 30	Asn	Gly	
cat His	tgc Cys	acc Thr 35	aag Lys	tat Tyr	gag Glu	ccc Pro	tgg Trp 40	cag Gln	cta Leu	att Ile	gca Ala	tgg Trp 45	agt Ser	gtc Val	gtg Val	144
tgg Trp	acc Thr 50	ctg Leu	ctg Leu	ata Ile	gtc Val	tgg Trp 55	gga Gly	tat Tyr	gag Glu	ttt Phe	gtc Val 60	ttc Phe	cag Gln	cca Pro	gag Glu	192
agt Ser 65	tta Leu	tgg Trp	tca Ser	agg Arg	ttt Phe 70	aaa Lys	aag Lys	aaa Lys	tgt Cys	ttt Phe 75	aag Lys	ctc Leu	acc Thr	agg Arg	aag Lys 80	240
atg Met	ccc Pro	att Ile	att Ile	ggt Gly 85	cgt Arg	aag Lys	att Ile	caa Gln	gac Asp 90	aag Lys	ttg Leu	aac Asn	aag Lys	acc Thr 95	aag Lys	288
gat Asp	gat Asp	att Ile	agc Ser 100	aag Lys	aac Asn	atg Met	tca Ser	ttc Phe 105	ctg Leu	aaa Lys	gtg Val	gac Asp	aaa Lys 110	gag Glu	tat Tyr	336
gtg Val	aaa Lys	gct Ala 115	tta Leu	ccc Pro	tcc Ser	cag Gln	ggt Gly 120	ctg Leu	agc Ser	tca Ser	tct Ser	gct Ala 125	gtt Val	ttg Leu	gag Glu	384
aaa Lys	ctt Leu 130	aag Lys	gag Glu	tac Tyr	agc Ser	tct Ser 135	atg Met	gac Asp	gcc Ala	ttc Phe	tgg Trp 140	caa Gln	gag Glu	Gly	aga Arg	432
gcc Ala 145	Ser	gga Gly	aca Thr	gtg Val	tac Tyr 150	agt Ser	Gly	gag Glu	gag Glu	aag Lys 155	ctc Leu	act Thr	gag Glu	ctc Leu	ctt Leu 160	480
gtg Val	aag Lys	gct Ala	tat Tyr	gga Gly 165	Asp	ttt Phe	gca Ala	tgg Trp	agt Ser 170	Asn	ccc Pro	ctg Leu	cat His	cca Pro 175	Asp	528
atc Ile	ttc Phe	cca Pro	gga Gly 180	Leu	cgc Arg	aag Lys	ata Ile	gag Glu 185	Ala	gaa Glu	att Ile	gtg Val	agg Arg 190	l ire	gct Ala	576
tgt Cys	tcc Ser	c ctg Leu 195	Phe	: aat : Asn	ggg Gly	gga Gly	cca Pro 200	Asp	tcg Ser	tgt Cys	gga Gly	tgt Cys 205	vaı	g act Thr	tct Ser	624
Gl <sup>y</sup>	g gga Gly 210	7 Thr	gaa Glu	ago Ser	ata Ile	cto Leu 215	Met	g gcc : Ala	tgc Cys	aaa Lys	a gca s Ala 220	a Cys	cgo Aro	g gat g Asp	ctg Leu	672
gcc Ala 225	a Phe	gaç e Glu	g aag 1 Lys	g Glž	j ato 7 Ile 230	. Lys	act Thi	cca Pro	ı gaa Glu	a att 1 Ile 23!	e Val	g gct L Ala	cco Pro	c caa o Glr	a agt Ser 240	720

gcc Ala	cat His	gct Ala	gca Ala	ttt Phe 245	aac Asn	aaa Lys	gca Ala	gcc Ala	agt Ser 250	tac Tyr	ttt Phe	gly ggg	atg Met	aag Lys 255	att Ile	768
gtg Val	cgg Arg	gtc Val	cca Pro 260	ttg Leu	acg Thr	aag Lys	atg Met	atg Met 265	gag Glu	gtg Val	gat Asp	gtg Val	agg Arg 270	gca Ala	atg Met	816
aga Arg	aga Arg	gct Ala 275	atc Ile	tcc Ser	agg Arg	aac Asn	act Thr 280	gcc Ala	atg Met	ctc Leu	gtc Val	tgt Cys 285	tct Ser	acc Thr	cca Pro	864
cag Gln	ttt Phe 290	cct Pro	cat His	ggt Gly	gta Val	ata Ile 295	gat Asp	cct Pro	gtc Val	cct Pro	gaa Glu 300	gtg Val	gcc Ala	aag Lys	ctg Leu	912
gct Ala 305	gtc Val	aaa Lys	tac Tyr	aaa Lys	ata Ile 310	ccc Pro	ctt Leu	cat His	gtc Val	gac Asp 315	gct Ala	tgt Cys	ctg Leu	gga Gly	ggc Gly 320	960
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ttt Phe	gat Asp	ttc Phe	cgg Arg 340	gtg Val	aaa Lys	ggt Gly	gta Val	acc Thr 345	agc Ser	att Ile	tca Ser	gct Ala	gac Asp 350	acc Thr	cat His	1056
aag Lys	ctg Leu	gaa Glu 355	aat Asn	atc Ile	aaa Lys	ggc Gly	atc Ile 360	ttt Phe	gtt Val	ttt Phe	ggg Gly	aat Asn 365	ccc Pro	caa Gln	ttg Leu	1104
tca Ser	ctc Leu 370	Ile	gct Ala	ctg Leu	gga Gly	tcc Ser 375	cgt Arg	gat Asp	ttt Phe	gac Asp	atc Ile 380	tac Tyr	cga Arg	cta Leu	tca Ser	1152
aac Asn 385	Leu	atg Met	act Thr	gct Ala	aag Lys 390	Gly	tgg Trp	aac Asn	ttg Leu	aac Asn 395	Gln	ttg Leu	cag Gln	ttc Phe	cca Pro 400	1200
ccc Pro	agt Ser	att Ile	cat His	ttc Phe 405	суѕ	atc Ile	aca Thr	tta Leu	cta Leu 410	cac His	gcc Ala	cgg Arg	aaa Lys	cga Arg 415	gta Val	1248
gct Ala	ata Ile	caa Glr	ttc Phe 420	e Leu	aag Lys	gac Asp	att Ile	cga Arg 425	Glu	tct Ser	gtc Val	act Thr	caa Gln 430	тте	atg Met	1296
aag Lys	aat Asn	cct Pro 435	Lys	gcç Ala	g aag Lys	acc Thr	aca Thr 440	Gly	atg Met	ggt Gly	gcc Ala	ato Ile 445	: Tyr	gcc Ala	atg Met	1344
gco	c caç	g aca	a act	gtt	gac	agg	aat	ato	gtt	gca	a gaa	ı ttç	g tec	tca	gtc	1392

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Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val
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ttc ttg gac agc ttg tac agc acc gac act gtc acc cag ggc agc cag
                                                                  1440
Phe Leu Asp Ser Leu Tyr Ser Thr Asp Thr Val Thr Gln Gly Ser Gln
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                   470
                                                                  1467
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Met Asn Gly Ser Pro Lys Pro His *
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His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val
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Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu
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Ser Leu Trp Ser Arg Phe Lys Lys Lys Cys Phe Lys Leu Thr Arg Lys
                                        75
                    70
Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys
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Asp Asp Ile Ser Lys Asn Met Ser Phe Leu Lys Val Asp Lys Glu Tyr
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Val Lys Ala Leu Pro Ser Gln Gly Leu Ser Ser Ser Ala Val Leu Glu
                            120
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Lys Leu Lys Glu Tyr Ser Ser Met Asp Ala Phe Trp Gln Glu Gly Arg
                                           140
                        135
Ala Ser Gly Thr Val Tyr Ser Gly Glu Glu Lys Leu Thr Glu Leu Leu
                   150
                                       155
Val Lys Ala Tyr Gly Asp Phe Ala Trp Ser Asn Pro Leu His Pro Asp
                                    170
                165
Ile Phe Pro Gly Leu Arg Lys Ile Glu Ala Glu Ile Val Arg Ile Ala
                                185
            180
 Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser
                            200
        195
Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Cys Arg Asp Leu
                        215
 Ala Phe Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Gln Ser
                                         235
                   230
Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile
                                    250
                245
 Val Arg Val Pro Leu Thr Lys Met Met Glu Val Asp Val Arg Ala Met
                                265
 Arg Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro
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280

```
Gln Phe Pro His Gly Val Ile Asp Pro Val Pro Glu Val Ala Lys Leu
                      295
Ala Val Lys Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly
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                 310
Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu His Pro
                                 330
              325
Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His
                   345
          340
Lys Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu
                          360
Ser Leu Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser
                               380
                      375
Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro
                                     395
                   390
Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val
                                  410
              405
Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met
          420 425
Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Ala Met
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    435
Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val
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Phe Leu Asp Ser Leu Tyr Ser Thr Asp Thr Val Thr Gln Gly Ser Gln
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Met Asn Gly Ser Pro Lys Pro His
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Val Leu Val Leu Ala Ala Phe Gly Gly Thr Leu Val Tyr Thr Lys Val
                          40
Val His Leu Tyr Arg Lys Ser Glu Asp Pro Ile Leu Lys Arg Met Gly
 Ala Tyr Val Phe Ser Leu Leu Arg Lys Leu Pro Ala Val Arg Asp Lys
                   70
Ile Glu Lys Glu Leu Ala Ala Glu Lys Pro Lys Leu Ile Glu Ser Ile
              85
                                   90
His Lys Asp Asp Lys Asp Lys Gln Phe Ile Ser Thr Leu Pro Ile Ala
                              105
 Pro Leu Ser Gln Asp Ser Ile Met Glu Leu Ala Lys Lys Tyr Glu Asp
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 Tyr Asn Thr Phe Asn Ile Asp Gly Gly Arg Val Ser Gly Ala Val Tyr
         135
 Thr Asp Arg His Ala Glu His Ile Asn Leu Leu Gly Lys Ile Tyr Glu
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Lys Tyr Ala Phe Ser Asn Pro Leu His Pro Asp Val Phe Pro Gly Ala
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              165
Arg Lys Met Glu Ala Glu Leu Ile Arg Met Val Leu Asn Leu Tyr Asn
                  185
Gly Pro Glu Asp Ser Ser Gly Ser Val Thr Ser Gly Gly Thr Glu Ser
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                       200
Ile Ile Met Ala Cys Phe Ser Tyr Arg Asn Arg Ala His Ser Leu Gly
                                      220
                    215
Ile Glu His Pro Val Ile Leu Ala Cys Lys Thr Ala His Ala Ala Phe
                     235
                 230
Asp Lys Ala Ala His Leu Cys Gly Met Arg Leu Arg His Val Pro Val
                  250
              245
Asp Ser Asp Asn Arg Val Asp Leu Lys Glu Met Glu Arg Leu Ile Asp
                            265
Ser Asn Val Cys Met Leu Val Gly Ser Ala Pro Asn Phe Pro Ser Gly
                         280
Thr Ile Asp Pro Ile Pro Glu Ile Ala Lys Leu Gly Lys Lys Tyr Gly
                                       300
         295
Ile Pro Val His Val Asp Ala Cys Leu Gly Gly Phe Met Ile Pro Phe
                         315
                 310
Met Asn Asp Ala Gly Tyr Leu Ile Pro Val Phe Asp Phe Arg Asn Pro
                                330
             325
Gly Val Thr Ser Ile Ser Cys Asp Thr His Lys Tyr Gly Cys Thr Pro
                            345
          340
Lys Gly Ser Ser Ile Val Met Tyr Arg Ser Lys Glu Leu His His Phe
                                          365
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<pre>&lt;400&gt; 18 Met Pro Ser Thr 1 Glu Ile Leu Glu 20 His Cys Thr Lys 35 Trp Thr Leu Leu 50 Ser Leu Trp Ser 65 Met Pro Ile Ile Asp Asp Ile Ser 100 Val Lys Ala Leu 115 Lys Leu Lys Glu 130 Ala Ser Gly Thr</pre>	Asp Leu 5 Val Tyr Tyr Glu Ile Val Arg Phe 70 Gly Arg 85 Lys Asn Pro Ser Tyr Ser Val Tyr 150	Ser The Addition of the Additi	hr Lys 25 rp Gln 0 ly Tyr ys Lys le Gln er Phe 105 ly Leu 20 et Asp	10 Ala Leu Glu Cys Asp 90 Leu Ser Ala Glu	Lys Ile Phe 75 Lys Ser Phe Lys 155	Asn Ala Val 60 Lys Leu Val Ser Trp 140 Leu	Tyr Trp 45 Phe Leu Asn Asp Ala 125 Gln Thr	Val 30 Ser Gln Thr Lys 110 Val Glu	15 Asn Val Pro Arg Thr 95 Glu Leu Gly Leu	Gly Val Glu Lys 80 Lys Tyr Glu Arg Leu 160	

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Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser
                         200
Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Tyr Arg Asp Leu
                     215
Ala Phe Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Gln Ser
                                   235
                 230
Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile
                   250
           245
Val Arg Val Pro Leu Thr Lys Met Met Glu Val Asp Val Arg Ala Met
                265
          260
Arg Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro
              280
                                285
Gln Phe Pro His Gly Val Ile Asp Pro Val Pro Glu Val Ala Lys Leu
                     295
                                        300
Ala Val Lys Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly
                                    315
                  310
Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu His Pro
              325
                                330
Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His
    340
                            345
Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Leu Val Leu Tyr Ser Asp
                         360
                                            365
       355
Lys Lys Tyr Arg Asn Tyr Gln Phe Phe Val Asp Thr Asp Trp Gln Gly
  370 375
                                        380
Gly Ile Tyr Ala Ser Pro Thr Ile Ala Gly Ser Arg Pro Gly Gly Ile
385 390
                                    395
Ser Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr
                                410
              405
Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser
                             425
Glu Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu
                         440
Ser Val Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser
                                        460
                     455
Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro
                                    475
                 470
Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val
              485
                                490
                                                  495
Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met
                            505
          500
Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met
                         520
                               525
Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val
                     535
Phe Leu Asp Ser Leu Tyr Ser Thr Asp Thr Val Thr Gln Gly Ser Gln
                 550
                                     555
Met Asn Gly Ser Pro Lys Pro His
               565
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<sup>&</sup>lt;210> 19

<sup>&</sup>lt;211> 490

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Drosophila melanogaster

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Phe Arg Ser Ser Asn Asp Tyr Gly Val Asn Leu Gln Thr Ala Glu Met
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Trp His His Thr Ile Arg Lys His Lys Arg Gly Asn Gly Ser Ser Ser
                              25
Pro Ala Asp Cys Gly Lys Gln Leu Leu Ile Leu Leu Asn Pro Lys Ser
                          40
Gly Ser Gly Lys Gly Arg Glu Leu Phe Gln Lys Gln Val Ala Pro Leu
                       55
Leu Thr Glu Ala Glu Val Gln Tyr Asp Leu Gln Ile Thr Thr His Pro
                                      75
                  70
Gln Tyr Ala Lys Glu Phe Val Arg Thr Arg Arg Asp Leu Leu Thr Arg
                                  90
               85
Tyr Ser Gly Ile Val Val Ala Ser Gly Asp Gly Leu Phe Tyr Glu Val
                               105
           100
Leu Asn Gly Leu Met Glu Arg Met Asp Trp Arg Arg Ala Cys Arg Glu
                           120
Leu Pro Leu Gly Ile Ile Pro Cys Gly Ser Gly Asn Gly Leu Ala Lys
                                           140
                      135
Ser Val Ala His His Cys Asn Glu Pro Tyr Glu Pro Lys Pro Ile Leu
                                      155
     150
His Ala Thr Leu Thr Cys Met Ala Gly Lys Ser Thr Pro Met Asp Val
                                  170
     165
Val Arg Val Glu Leu Ala Thr Arg Asp Lys His Phe Val Met Tyr Ser
                              185
           180
Phe Leu Ser Val Gly Trp Gly Leu Ile Ala Asp Ile Asp Ile Glu Ser
                                              205
                           200
        195
Glu Arg Leu Arg Ser Ile Gly Ala Gln Arg Phe Thr Leu Trp Ala Ile
                       215
Lys Arg Leu Ile Gly Leu Arg Ser Tyr Lys Gly Arg Val Ser Tyr Leu
                                       235
                   230
Leu Gly Lys Gly Lys Glu Pro Pro Val Glu Ala Ala Arg Glu Leu
                                   250
               245
Pro Ala Glu Ser Thr Ala Ala Gly Ile Arg Ser Ser Leu Pro Leu Asn
                                     270
                              265
            260
Ala Gly Glu Phe His Asp Leu Pro Glu Glu Glu Glu Gly Glu Ala Val
                           280
Leu Asp Gly Glu Gln Phe Ala Asp Ala Ile Ser Leu Asp Arg Ser Val
                      295
                                           300
Tyr Arg Gln His Ala Asp Ser Trp His Ser Ala Met Ser Arg Arg Thr
                                      315
                   310
Ala Tyr Tyr Ser Leu Gly Gly Pro Ser Met Arg Ser Asn Arg Ser Arg
                                   330
                325
Met Ser Ile Ser Gln Arg Ile Glu Ala Ala Asn Ala Glu Phe Ala Glu
                               345
Arg Val Pro Thr Gly Thr Ile Pro Pro Leu Gln Met Pro Leu Leu Ser
                            360
Ser Asp Gly Trp Ile Cys Glu Asp Gly Asp Phe Val Met Val His Ala
                                           380
                       375
Ala Tyr Thr Thr His Leu Ser Ser Asp Val Phe Phe Ala Pro Glu Ser
                                      395
                   390
Arg Leu Asp Asp Gly Leu Ile Tyr Leu Val Ile Ile Arg Arg Gly Val
                405
                                   410
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Ser Arg His Gln Leu Leu Asn Phe Met Leu Asn Leu Asn Ala Gly Thr
                              425
           420
His Leu Pro Ile Gly Glu Asp Pro Phe Ile Lys Val Val Pro Cys Arg
                          440
Ala Phe Arg Ile Glu Pro Ser Ser Ser Asp Gly Ile Leu Val Val Asp
                                         460
                      455
Gly Glu Arg Val Glu Tyr Gly Pro Ile Gln Ala Glu Val Met Pro Gly
                              475
               470
Leu Ile Asn Val Met Thr Thr Ser Gly Gln
               485
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<210> 20 <211> 524 <212> PRT <213> Drosophila melanogaster

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Val Ile Ser Leu Glu Thr Ser Ile Asn Gln Ser Phe Arg Ser Arg Cys
                       295
Asp Ser Trp Leu Ser Gly Gly Ser Arg Arg Ser Phe Tyr Tyr Ser Ile
                   310
                                       315
Ser Glu Ser Ile Tyr His Ser Leu Ala Asp Glu Ser Glu Phe Ala Gly
                                  330
               325
Leu Ala Ala Ala Ser Leu Glu Asn Arg Gln Gln Asn Tyr Gly Pro Ala
                              345
           340
Ser Glu Leu Pro Asp Leu Asn Glu Pro Leu Ser Glu Asp Gln Gly Trp
                                            365
                           360
Leu Val Glu Glu Gly Glu Phe Val Met Met His Ala Val Tyr Gln Thr
                                          380
                       375
His Leu Gly Ile Asp Cys His Phe Ala Pro Lys Ala Gln Leu Asn Asp
                                       395
                   390
Gly Thr Ile Tyr Leu Ile Leu Ile Arg Ala Gly Ile Ser Arg Pro His
                                   410
                405
Leu Leu Ser Phe Leu Tyr Asn Met Ser Ser Gly Thr His Leu Pro Glu
                                                   430
                               425
Ser His Asp Asp His Val Lys Val Leu Pro Val Arg Ala Phe Arg Leu
                           440
       435
Glu Pro Tyr Asp Asn His Gly Ile Ile Thr Val Asp Gly Glu Arg Val
                       455
                                           460
Glu Phe Gly Pro Leu Gln Ala Glu Val Leu Pro Gly Ile Ala Arg Val
                                      475
                   470
Met Val Pro Asn Val Ser Thr Phe Arg Phe Gln Ser Ala Thr Leu Gln
                                  490
               485
His Gly Ile Pro Val Cys Ile Pro Val Arg Lys Arg Phe Val Leu Tyr
                               505
Asn Met Ser Ser Glu Glu Leu Ala Pro Ile Asn Glu
                            520
<210> 21
<211> 368
<212> PRT
<213> Homo sapiens
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Val Leu Val Leu Leu Asn Pro Arg Gly Gly Lys Gly Lys Ala Leu Gln
                                    10
                5
Leu Phe Arg Ser His Val Gln Pro Leu Leu Ala Glu Ala Glu Ile Ser
                               25
            20
Phe Thr Leu Met Leu Thr Glu Arg Arg Asn His Ala Arg Glu Leu Val
                            40
Arg Ser Glu Glu Leu Gly Arg Trp Asp Ala Leu Val Val Met Ser Gly
                        55
Asp Gly Leu Met His Glu Val Val Asn Gly Leu Met Glu Arg Pro Asp
                                        75
                   70
Trp Glu Thr Ala Ile Gln Lys Pro Leu Cys Ser Leu Pro Ala Gly Ser
                85
                                   90
Gly Asn Ala Leu Ala Ala Ser Leu Asn His Tyr Ala Gly Tyr Glu Gln
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105 Val Thr Asn Glu Asp Leu Leu Thr Asn Cys Thr Leu Leu Cys Arg 120

Arg Leu Leu Ser Pro Met Asn Leu Leu Ser Leu His Thr Ala Ser Gly 135 140 Leu Arg Leu Phe Ser Val Leu Ser Leu Ala Trp Gly Phe Ile Ala Asp 155 150 Val Asp Leu Glu Ser Glu Lys Tyr Arg Arg Leu Gly Glu Met Arg Phe 170 165 Thr Leu Gly Thr Phe Leu Arg Leu Ala Ala Leu Arg Thr Tyr Arg Gly 180 185 Arg Leu Ala Tyr Leu Pro Val Gly Arg Val Gly Ser Lys Thr Pro Ala 200 205 Ser Pro Val Val Val Gln Gln Gly Pro Val Asp Ala His Leu Val Pro 220 215 Leu Glu Glu Pro Val Pro Ser His Trp Thr Val Val Pro Asp Glu Asp 235 230 225 Phe Val Leu Val Leu Ala Leu Leu His Ser His Leu Gly Ser Glu Met 250 245 Phe Ala Ala Pro Met Gly Arg Cys Ala Ala Gly Val Met His Leu Phe 270 265 Tyr Val Arg Ala Gly Val Ser Arg Ala Met Leu Leu Arg Leu Phe Leu 275 280 Ala Met Glu Lys Gly Arg His Met Glu Tyr Glu Cys Pro Tyr Leu Val 295 300 Tyr Val Pro Val Val Ala Phe Arg Leu Glu Pro Lys Asp Gly Lys Gly 310 315 Val Phe Ala Val Asp Gly Glu Leu Met Val Ser Glu Ala Val Gln Gly 330 335 325 Gln Val His Pro Asn Tyr Phe Trp Met Val Ser Gly Cys Val Glu Pro 345 340 Pro Pro Ser Trp Lys Pro Gln Gln Met Pro Pro Pro Glu Glu Pro Leu 365 360